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A relative ranking approach for nano-enabled applications to improve risk-based decision making: a case study of Army materiel

Khara D. Grieger · Jennifer Hoponick Redmon · Eric S. Money · Mark W. Widder · William H. van der Schalie · Stephen M. Beaulieu · Donna Womack

Abstract Assessing the health and environmental risks of engineered nanomaterials (ENMs) continues to be a challenging endeavor. Due to extensive challenges related to applying traditional risk assessment frameworks to ENMs, decision making regarding the use of ENMs in products and applications may need to rely on structured decision support tools such as risk ranking approaches. This study examines the use of one risk ranking tool that incorporates both quantitative and qualitative information regarding the potential human health risks of ENMs, focused primarily on worker and soldier health. Using a case study involving Army materiel (i.e., equipment), a relative risk ranking algorithm is proposed that accounts for not only the physicochemical characteristics of the ENMs, but also the characteristics of the Army materiel. In this way, the resulting risk potential for soldiers and workers is not solely based on the inherent characteristics of the ENMs but is also influenced within the context of the technology being developed. Among other important findings, the results from applying this risk ranking algorithm in this case study suggest that inhalation from accidental exposures to carbon nanotubes and copper flakes incorporated into energy and obscurant materiel by Army workers rank highest relative to the other items evaluated in this baseline assessment. As the presence of data gaps was one of the greatest challenges to applying this risk ranking algorithm, future applications may benefit from reliance on a continually revised database that may be updated in real time and possibly synced with publically available databases in order to use the most current and comprehensive set(s) of data available.

Keywords Army materiel · Engineered nanomaterials · Nanotechnology · Relative risk ranking · Risk assessment

1 Introduction

Assessing the potential human health and environmental risks of engineered nanomaterials (ENMs) within the context of the applications and products in which they are incorporated continues to be an extremely challenging endeavor. A decade after the UK Royal Society released their 2004 report (Dowling et al. 2004), scientists, researchers, governments, institutions, and industry still grapple with the multitude of uncertainties and data gaps associated with characterizing the potential ENM hazards and formulating effective strategies to handle these

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K. D. Grieger (✉) · J. H. Redmon · E. S. Money · S. M. Beaulieu · D. Womack
Center for Health and Environmental Modeling, RTI International, 3040 East Cornwallis Rd., Research Triangle Park, Durham, NC 27709-2194, USA
e-mail: kgrieger@rti.org

M. W. Widder · W. H. van der Schalie
Center for Environmental Health Research, United States Army, Fort Detrick, Frederick, MD 21702-5010, USA

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14. ABSTRACT
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15. SUBJECT TERMS
Army materiel, engineered nanomaterials, nanotechnology, relative risk ranking, risk assessment

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potential risks. Given the challenges of developing sufficient data that would be required for traditional risk assessment frameworks (e.g., Choi et al. 2009), risk assessors are continuing to refine their methods and techniques to perform risk assessments using combined quantitative and qualitative frameworks for ENMs, resulting in various alternatives for risk analysis (e.g., DuPont 2007; Tervonen et al. 2009; Canis et al. 2010; TUV/SUD 2012; Grieger et al. 2012). Among some of these risk analysis methods, a number of risk ranking tools and methods have been developed and demonstrated for ENMs or related processes and applications (Tervonen et al. 2009; Canis et al. 2010; Linkov and Seager 2011; Linkov et al. 2013). The use of risk ranking tools may be particularly advantageous to prioritize materials or products according to their risk potential, i.e., identify the "riskiest" ENMs or nano-products, for example, for further research or investigation. This may be useful especially in cases of resource and time constraints.

Based on the research conducted by the US Army Center for Environmental Health Research (USACEHR) associated with the incorporation of various ENMs into military applications (termed "Army materiel"), this analysis develops and implements a risk ranking tool to rank ENM–Army materiel pairs based on their relative risks to soldier and civilian health under occupational scenarios. The USACEHR has been conducting research and development efforts on the incorporation of various ENMs into Army materiel, ranging from food storage to computer systems and weaponry (Kharat et al. 2006; Turaga et al. 2012). With such a wide range of ENMs being incorporated into a variety of materiel, the US Army has proactively engaged in efforts to identify the ENMs and ENM–Army materiel applications that constitute the largest potential health risk for soldiers using the materiel and for civilian workers developing the materiel.

This project therefore aimed to (1) identify and inventory the ENMs and their associated applications in Army materiel, (2) develop a risk ranking algorithm that takes into account both ENM and materiel characteristics, and (3) apply the algorithm and associated risk ranking tool to prioritize additional assessments based on the human health risk potential related to ENMs, Army materiel, and ENM–materiel pairs. This study is unique in that real-world ENM–Army material pairs used in research or full-scale field applications were considered to perform the relative risk ranking rather than primarily hypothetical or pristine ENMs. Based on the results of this analysis, recommendations are provided for the further development of risk ranking tools specifically for ENMs in order to facilitate sound decision making regarding these novel materials in diverse applications.

2 Methodology

2.1 Develop inventory of ENMs and Army materiel

First, an inventory of ENMs used in Army research and field applications (i.e., Army materiel) was developed. This inventory was incorporated into a database linking the ENMs and materiel applications to form ENM–materiel pairs. To generate an inventory of ENMs and Army materiel, 16 subject matter experts provided by the US Army were interviewed to obtain information on the identity, use, and materiel application of ENMs. Telephone interviews and online e-mail questionnaires were used to collect information on the ENMs and Army materiel, with the completion of several follow-up interviews and online correspondence to confirm, edit, and supplement the inventory with additional information (See Section 1 in Supplementary Information (SI) for questionnaires used in the interview process).

2.2 Identification of ENM characteristics

After producing a complete inventory of ENMs and Army materiel (available in Table S1 in SI), the physicochemical characteristics of the ENMs were developed for risk ranking purposes (Table 1). A total of 27 characteristics of ENMs were used, based on the current literature pertaining to the health and environmental risks of ENMs, scientific expertise in ENM behavior and toxicology, information provided by the Army, and general consideration of potential risks for civilian workers and soldiers from exposures to ENMs (e.g., Thomas and Sayre 2005; Boxall et al. 2007; Auffan et al. 2009; Chappell 2009; Oberdörster 2010). For organization purposes as well as for later use for risk ranking, these ENM characteristics were grouped into five different categories which describe the ENM and/or its behavior: fate, reactivity, structure, chemistry, and application-specific characteristics. These ENM characteristics and groupings all relate to three risk factors: (1) ENM release potential (i.e., the likelihood that a certain ENM concentration or mass could enter an environmental compartment, such as air, water, soil/sediment, during operational or accidental use of the Army materiel in which it is embedded), (2) ENM exposure potential (i.e., the likelihood that a soldier or civilian worker could come into contact via dermal, inhalation, and/or ingestion pathways with the ENM released from an Army materiel, and (3) ENM toxicity potential (i.e., the likelihood that a receptor could develop adverse effects from the release and subsequent exposure to the ENM in question). These aforementioned risk factors (i.e., ENM release, exposure, and toxicity potentials) all affect the relative rankings of ENM–materiel pairs. Table S2 in SI provides

Table 1 List of ENM physicochemical characteristics used in this analysis

Category	ENM characteristic	Definition
Fate	Degradation potential	The ability of the ENM to be decomposed/dissolved by bacteria or other biological means. Representative of "Fate" due to its ability to cover other ENM characteristics in "Fate" and lack of available data for other characteristics in this category
	Dispersibility	The ability of the ENM to become distributed continuously throughout a particular medium (in this case air)
	K_{oc}	Organic carbon–water partitioning coefficient; represents the ability of the ENM to adsorb to organic carbon and move through carbon-rich environments
	K_{ow}	Octanol–water partitioning coefficient; represents the tendency to sorb to non-polar, lipophilic compounds (lower Kow – > more soluble – > less sorbing to solids)
	Persistence	The ability of the ENM to remain in the environment without modification (e.g., biodegradation)
	Bioaccumulation	The ability of the ENM to accumulate in the tissues of organisms
	Half-life	The amount of time it takes for ENM activity to be reduced by half (or concentration reduced by half)
Reactivity	Toxicity	The potential for adverse health effects, if exposed to a given ENM. Representative of "Reactivity" due to its ability to cover other ENM characteristics in "Reactivity" and importance to understanding its behavior with biological systems
	Surface charge/zeta potential	The electric charge present at the interface between two particles. Zeta potential represents the degree of repulsion between adjacent, similarly charged particles. Larger absolute zeta potentials lead to more stability in solutions. Representative of "Reactivity" due to its importance to understanding its behavior with biological systems particularly relevant for ENMs
	Surface reactivity	The ability of the ENM surface to interact with other particles. Generally a function of other properties such as surface charge/zeta potential, shape, surface area, and surface chemistry
	Radical formation	The ability of ENM to cause a release of free radicals
	Catalytic reaction	The ability of ENM to enable or enhance reactions
	Flammability	The ease at which ENM could ignite or burn, thereby causing fires or combustion reactions during use
	Explosivity	The tendency of ENM to explode
Structural	Particle size	The typical (modal) diameter for a distribution of raw ENM (often there is a size distribution, rather than one distinct size). Representative of "Structural" due to the relevance for ENMs and more often reported in the literature compared to some of the other ENM characteristics in this category
	Density	The mass of ENM per unit volume
	Composition	The chemical constituents that make up the ENM
	Surface area	The surface area of the ENM in square meters (or nanometers)
	Molecular structure	The molecular formula of the ENM, including the bond structure and strength
	Porosity	A measure of the 'empty' spaces in a materiel as volume
	Crystallinity	The degree of ordered structures in the materiel (closely related to porosity and molecular structure)
	Dustiness	The likelihood of ENM becoming airborne during use or disturbance
Chemistry	Solubility	The ability of the ENM to dissolve in a solid, liquid, or gaseous solvent. Representative of "Chemistry" due to its importance in chemical interactions as well as exposure potential with biological systems
	Aggregation	The ability of individual ENM (nanoparticle) to physically/chemically combine into larger particles (related to agglomeration/flocculation)
	Surface chemistry	The properties that affect chemical interactions between two surfaces. In this instance, the presence and composition of surface coatings on the ENM
Application-specific	Form	The physical configuration of the ENM at their final use (e.g., particles, bulk, sheets, fibers, etc.). Representative of "Application-Specific" due to its importance in determining exposure and hazard potentials, in which different forms may produce different responses for certain ENMs
	Shape	The normal physical appearance of the raw ENM (e.g., tubes and spheres). Representative of "Application-Specific" due to its importance in determining exposure and hazard potentials, in which different shapes may produce different responses for certain ENMs

Note that the ENM characteristics shown in bold below were those chosen as being representative of each category, a designation that was useful for data collection and risk scoring purposes

additional details on how the 27 ENM characteristics relate to each of these three risk factors. Other authors, such as Epa et al. 2012, Winkler et al. 2013, and Meesters et al. 2014, provide more details on how ENM physicochemical parameters (characteristics) relate to toxicological effects and exposure pathways.

2.3 Identification of Army materiel characteristics

As the relative health risks considered in this case study pertain to ENMs used in specific Army materiel applications, Army materiel characteristics were also identified that may play a significant role in determining the relative risk of the pairs of ENMs and the materiel in which they are embedded. Overall, ten Army materiel characteristics were defined using data from the Army (Table 2). Seven of the materiel characteristics were used in scoring, relevant for risk ranking purposes, while three characteristics were only used for informational purposes.

2.4 Data acquisition and expert elicitation for ENMs and Army materiel characteristics

To streamline the data acquisition process as well as handle the numerous data gaps associated with information on each of the 27 ENM characteristics, a total of seven ENM characteristics were selected as being representative of each ENM category. These representative ENM characteristics are shown in bold in Table 1 and include degradation potential, surface charge/zeta potential, toxicity, particle size, solubility, form, and shape. Quantitative values (e.g., solubility) or qualitative information (e.g., form) was obtained for these seven representative characteristics using available Army-supplied or literature-based data. These values were subsequently incorporated in the scoring process to produce semi-quantitative scores for each ENM (see subsequent section as well as Table S2 in SI for details) and served as surrogate data for the other characteristics in each respective ENM characteristic category. For example, data or information collected either from the Army or the literature pertaining to the degradation potential of a particular ENM would be used as representative data (denoted as "representative" in the characteristic scoring basis, see Table S2 in SI) for other ENM characteristics in the "fate" ENM characteristics category such as, e.g., dispersibility and Koc (denoted as "default" in the characteristic scoring basis, Table S2). This was due primarily to the challenges of obtaining data for all 27 ENM characteristics and therefore served as a way to manage the data gaps in the data collection process. As noted in subsequent sections, there is also a built-in functionality to the database to add and update additional information and data for the ENM characteristics, including the non-representative ENM characteristics, as information becomes available.

Table 2 List of Army materiel characteristics used in this analysis

Materiel characteristic	Definition
Amount	The amount (%) of ENM incorporated into the materiel (relates to release potential, exposure potential) (e.g., a materiel containing a very small % of ENM would be less likely to release the ENM and would result in a smaller exposure concentration)
Number end items	The total number of individual final (produced) items for a particular ENM–materiel pair (relates to exposure potential), e.g., if 5,000 end items are produced, the likelihood of exposure is greater than a materiel with currently only two end items
Number people exposed	The total number of current individuals with the potential for exposure to the ENM-containing materiel (relates to exposure potential), e.g., if three people have the potential for exposure due to current use, rather than thousands, then exposure potential is considered low
Acquisition phase	The current status of the ENM-containing materiel based on life cycle stage, from concept design to production and deployment (relates to exposure potential) [e.g., a materiel that is still in the concept design phase (e.g., planning only) would have no exposure potential, whereas a materiel that has been deployed for use could potentially have a large exposure potential]
Use patterns	A descriptor for who will primarily be using the ENM-containing materiel in its current stage and in what setting (relates to release, exposure potential, and toxicity potential), e.g., an ENM used in an obscurant would theoretically have a higher release, exposure, and toxicity potential than an ENM used in body armor
Incompatibility	A list of substances that may be incompatible with the ENM-containing materiel
Method of incorporation	A descriptor for how the ENM is incorporated into the materiel (i.e., on the surface, in a polymer matrix, in a powder, etc.) relates to release, exposure, and toxicity potential, e.g., if the ENM is present in a polymer matrix, then the likelihood of release and subsequent exposure/toxicity would be diminished
Toxicity clearance[a]	Yes/no answer on whether or not a toxicity clearance has been performed for the materiel application containing ENMs
MSDS[a]	Yes/no answer representing the presence/absence of a material safety data sheet for the ENM used in the application
Health hazard assessment[a]	Yes/no answer on whether or not a health hazard assessment has been performed on the materiel application containing the ENMs

[a] Note that these three Army materiel characteristics were not used in risk ranking but served as additional descriptive information

A hierarchical approach was used to acquire data for each of the seven representative ENM characteristics. First, the Army supplied the first round of data attributed to the ENMs and Army materiel, and then, publically available literature was subsequently used to help fill in the remaining data gaps. Throughout the data collection period, the Army provided data and information for only 39 % of the ENM-materiel pairs. Therefore, the literature in the form of Material Safety Data Sheets (MSDSs) as well as scientific journals was accessed subsequently. A MSDS typically provides some information on the ENM or bulk materials, e.g., particle size, shape, solubility, and toxicity, although there was significant variability in the type and quantity of information provided between MSDSs. Furthermore, follow-up communication with the ENM manufacturer used by Army personnel was also conducted in some instances in order to obtain as much information as possible from an MSDS. Then, for information that could not be found using MSDSs, existing scientific literature was used to ascertain necessary data or descriptive information on toxicity and surface charge/zeta potentials. Several literature values were examined to account for some of the variability in ENMs used across different studies. If ENM-specific data could not be found, bulk-scale characteristics of the primary constituent were collected from a corresponding MSDS to serve as a placeholder until ENM-specific data become available. Finally, for the data gaps that could not be addressed due to a lack of scientific literature, existing chemical databases including EPA EpiSuite (USEPA 2014) and ChemSpider (Pence and Williams 2010) were used to obtain initial values, often based on information related to bulk-scale materials.

These data and information were collected and incorporated into the underlying database of the risk ranking tool, Tool for ENM Application pair Risk Ranking (TEARR). TEARR was designed with Microsoft Office 2007 with Visual Basic 6.5 code and implemented using an access database with a corresponding user interface (see Figures S1–S4 in SI for screenshots). The underlying database in TEARR therefore served as the source of underlying data used for an expert elicitation of the ENM risk factor scores for each representative ENM characteristic as well as Army materiel impact scores as explained below.

In an expert elicitation process, two prominent nanotoxicologists were used to elicit scores (i.e., 1, 3, and 5) for the three ENM risk factors (release potential, exposure potential, and toxicity potential) for each of the representative ENM characteristics based on the data collected (see SI for more details). To assign a score to a particular ENM risk factor related to a given ENM–materiel pair, the following question was posed: "For each inherent ENM characteristic associated with a given ENM-materiel pair, based on a given value for the ENM characteristic, what is the release potential, exposure potential, and/or toxicity potential of the ENM–materiel pair?" An ENM risk factor score of 1 relates to a low potential, 3 medium potential, and 5 high potential. The ranking scale of 1, 3, and 5 was chosen based on its use in other risk ranking analyses for ENMs, such as Höck et al. (2008), and was deemed a simple approach to qualitatively assign low-, medium-, and high-risk potentials. The individual ENM risk score represents the relative risk that a particular ENM characteristic will have on each ENM risk factor. For the other ENM (non-representative) characteristics, scoring rules were used to provide the scores for the risk factors (see Table S2 in SI), whereby default scores were assigned to the remaining the ENM characteristics in each ENM characteristic category. See Section 4 in SI for full details of the expert elicitation process.

Similar to eliciting scores of ENM risk factors, expert elicitation was also used to assign Army materiel impact scores for each Army materiel characteristic. An Army materiel impact score represents the impact that a particular materiel characteristic will have on the total risk of an ENM–material application pair, and values of 0, 0.5, 1, 2, 5, 10, or 100 were used. A materiel impact score of 0 indicates that ENM used in this Army materiel is expected to negate the overall risk of the application pair for a specific receptor/exposure (e.g., for soldiers wearing body armor, it is expected that there is no risk because release of the ENM is not expected to occur given the Method of Incorporation). An impact score of 0.5 indicates that the ENM used in the Army materiel is expected to decrease the overall risk of the ENM–materiel pair for a specific scenario by a factor equal to the impact score, although the ENM is still considered to pose some risk related to potential release into the environment and exposing receptor populations. Impact score of 1 indicates that ENM used in the Army materiel may or may not influence the overall risk of the ENM–materiel pair for a specific scenario, or no data/information (i.e., no information supplied by Army for materiel). Impact score >1 (i.e., 2, 5, 10, or 100) indicates that the ENM used in the Army materiel is expected to increase the overall risk of the ENM–materiel pair by a factor equal to or greater than the materiel impact score (e.g., if the number of people potentially exposed is in the thousands, this would be considered substantial relative to the current Army-supplied data; thus, the materiel impact score for the 'number of people exposed' materiel characteristic would be >1). Average Army materiel impact scores were derived by averaging the materiel impact scores for all Army materiel characteristics and indirectly relate to the release, exposure, and toxicity potential of a particular application.

After ENM risk factors were assigned through the expert elicitation process, ENM risk factor scores were weighted

by the experts in order to increase or decrease the relative importance of certain ENM characteristics which may be more uncertain or of lesser importance compared with others. Because there is still substantial uncertainty to understanding the potential release, exposure, and toxicity potential of ENMs in various applications, the user has the ability to adjust the ENM weights in the risk ranking algorithm (w1, Eq. 1). This weighting scheme also has the advantage of providing valuable information on the sensitivity of the ranking results, whereby the user can compare the ranking results when using different weights for ENM risk factor scores. Similar to assigning ENM risk scores, a binning system was used (i.e., 0, 1, 2) to assign a weight to each ENM characteristic by the experts based on the following question: "How significant to the overall relative riskiness of the ENM–materiel pair is the release potential, exposure potential, and/or toxicity potential due to this ENM characteristic?" A weight of 0 relates to not significant, 1 moderately or equally significant to other ENM risk factor scores, and 2 very or more significant than other ENM risk factor scores. A default weight of 1 was used in the baseline set of results. Average ENM risk factor scores were then determined by first multiplying each ENM risk factor score by its corresponding weight, then summing the weighted score for each characteristic chosen by the user, and dividing by the total number of characteristics chosen.

Several assumptions were made to relate the three ENM risk factors to the overall risk of an ENM–Army materiel pair. First, it was assumed that the ENM–materiel pair cannot pose a risk to a receptor if exposure does not occur. Similarly, it was assumed that exposure is not likely if the ENM is not released into an environment from the Army materiel. It was also assumed that a direct toxicity characteristic for the Army materiel would thereby increase the toxicity scoring for an individual ENM. For this, the use of Army materiel characteristics, such as Method of Incorporation and Use Patterns, appropriately will allow the adjustment of the overall toxicity of the Army materiel and subsequent relative risk score by considering how the ENM is being used in the materiel (e.g., Can the ENM be released from the materiel? Can the receptor subsequently be exposed to the ENM and can health effects then occur from exposure?). Finally, potential exposures through waste or other end-of-life cycle stages were not included in the present study.

2.5 Relative risk ranking parameters and ranking algorithm

After collecting data and information on ENMs, Army materiel, and eliciting ENM risk factor and Army materiel impact scores, this information was incorporated into a relative risk ranking algorithm within TEARR (Eq. 1). The outcome of the risk ranking algorithm produces relative risk results that identify the higher risk ENMs, Army materiel, and ENM-materiel pairs according to receptor type, release type, and exposure route based on the scenario selected by the user. Overall, the relative risk of a particular ENM–materiel pair is calculated based on the average ENM risk score multiplied by the average Army materiel impact score.

The relative risk score, R, for a user profile, i, and release profile, j, is calculated in Eq. 1 as follows for a specific ENM–Army materiel pair. An example calculation using Eq. 1 can also be found in Supplementary Information (Section 5).

$$R_{h,i,j} = \sum_{1}^{m} \left[\frac{1}{n1} \sum_{1}^{n1} \left(\mathrm{RS}_{k1,m} \cdot w_{k1,m} \right) \right] \cdot \left[\frac{1}{n2} \sum_{1}^{n2} \mathrm{IS}_{k2} \right] \tag{1}$$

where:h = [dermal, ingestion, inhalation];i = [civilian worker, soldier];j = [occupational, accidental];m = [1, 2, or 3] and corresponds to the risk factors (release potential, exposure potential, or toxicity potential) for a particular ENM characteristic, k1;$n1$ = the total number of ENM characteristics ranked by the user;RS = [1, 3, or 5] and is the relative risk score for a particular ENM characteristic, k1, and risk factor, m;$k1$ = ENM characteristic$w1$ = [0, 1, or 2] and corresponds to the ranking weight assigned by the user;$n2$ = the total number of Army materiel characteristics;IS = [0, 0.5, 1, 2, 5, 10, or 100] and corresponds to the user-weighted materiel impact score for a particular Army materiel characteristic, k2;$k2$ = Army materiel characteristic

2.6 Running scenarios and viewing results

In order to generate the baseline results of the data and information contained within TEARR, the user first creates the scenario of interest. In this step, the user first selects the receptor (i.e., soldier, worker), release type (i.e., accidental, operational), and exposure route (i.e., dermal, ingestion, inhalation) of interest (Figure S1 in SI shows a screenshot of this setup screen in TEARR). Next, the user selects the Army materiel and ENMs (see Table S1 in SI for a complete list of ENMs and materiel). Note that only the ENMs included in the selected Army materiel will be available for selection in TEARR, i.e., TEARR relies on specific ENM–materiel pairs. The user also selects the ENM characteristics of interest (see Table 1). Next, the user is able to view and adjust the Army materiel impact scores (default value is set to 1 if no prior impact score has been entered previously, and a default weight of 1 was used in the baseline set of results; see Figure S2 in SI) as well as ENM scores and weights (see Figure S3 in SI). Then, the user runs the scenario in order to generate the relative risk ranking scores

and output. On this results screen (not shown for confidentiality reasons; i.e., Army-sensitive related information), the user is able to view the ENM risk scores, Army materiel impact scores, relative risk score, and relative risk rank for the ENM–materiel pairs. In essence, the results from TEARR show not only a ranked list of the ENM–materiel pairs but also results based solely on the ENM or Army materiel type. Finally, the summary results screen (see Figure S4 in SI) provides an overview of the relevant receptor, release and exposure types, average Army materiel impact scores, average ENM risk score, as well as overall relative risk scores listed in descending order.

In addition to viewing the relative risk ranking results of ENMs, Army materiel, and ENM–materiel pairs, the user is also able to view the data sources used to determine the ENM risk scores and Army materiel impact scores (i.e., Army supplied, literature based, expert elicitation, and default scoring based on scoring rules shown in Table S2) on a separate screen within TEARR (Figure S5 in SI). The user is also able to view supplemental information which was provided by the Army but not incorporated into the TEARR algorithm in order to view any additional information related to Army materiel characteristics that may be relevant to the selected scenario. This is listed under the "supplemental info" table (not shown here).

2.7 Updating data and information within TEARR

TEARR has the ability to evolve and adapt to the incorporation of new information as well as expert knowledge. Users are currently able to modify the Army material impact scores as well as ENM risk factor scores and weights if she/he is aware of additional information not currently included in the underlying database within TEARR. TEARR also has the ability for users to modify the default risk scores used in the underlying scoring scheme as more information and data become available.

3 Results and discussion

3.1 ENM and Army materiel inventory

A total of 45 ENMs, 30 Army materiel applications, and 133 separate ENM–Army materiel pairs were identified in this analysis. The ENMs were grouped into seven categories based on their composition: carbon-based, inorganic, metals, metal oxides, quantum dots, other, and unknown (see Table S1 in SI). The Army materiel was grouped into six categories based on their functionality and use: chemicals, electronics, equipment, munitions, support, and structural material (Table S1 in SI). Figure 1 shows the distribution of ENMs across the ENM–materiel pairs ($N = 133$), revealing that carbon nanotubes (CNT) make up the largest number of Army materiel applications ($N = 13$), followed by silver (Ag), gold (Au), aluminum (Al), and alumina (Al_2O_3) (all with $N = 6$). While a full list of ENMs and Army materiel is listed in Table S1 of Supplementary Information (SI), a complete list of all ENM–Army materiel pairs is not provided in this analysis due to sensitive nature of this information.

3.2 Relative risk scores

Given the various options that users may select when setting up a given scenario (i.e., receptors types, release types, three exposure routes, ENMs, and materiel), there were 1,596 different scenarios possible for ranking in TEARR. Based on the risk ranking algorithm, the relative risk scores can potentially range from 0 to 3,000, with 3,000 representing the ENM–materiel pair with the highest relative risk score. To place this within context, the components of the relative risk score include the average ENM risk score (which can range 1–30) and the average Army materiel impact score (which can range 0–100). Figure 2 illustrates the final relative risk scores for all 1,596 scenarios along with each ENM risk score and Army materiel impact score.

Although there is the possibility for a risk score to reach 3,000, the highest achieved score based on current knowledge for the ENMs and Army materiel in TEARR was 42.84 (Table 3). This is most likely due to the fact that the baseline Army materiel impact scores did not include the highest potential scores (e.g., 10, 100) for most ENM–materiel pairs given the high degree of uncertainty regarding the maximum values possible for a given Army materiel characteristic. To investigate this further, the values of 10 and 100 were excluded from the Army materiel impact scores in a separate analysis, which resulted in the overall maximum final risk score adjusted to 150. Therefore, the likely cause of the relatively low maximum risk score compared with a theoretical maximum is due to the relatively low Army materiel impact scores used in the TEARR baseline analysis.

3.3 Risk ranking results

Baseline results from TEARR showed the relative rankings of Army materiel, ENMs, as well as ENM–Army materiel pairs. Looking at the individual ENM–materiel pairs, the baseline risk ranking results show that aluminum (Al), copper (Cu), and titanium (Ti) flakes used in smokes and obscurants ranked the highest on the risk scale for scenarios primarily involving accidental civilian worker and/or soldier inhalation (data not shown for confidentiality reasons). Due to the anticipated number of end items and potential for many people to be exposed, the dermal and

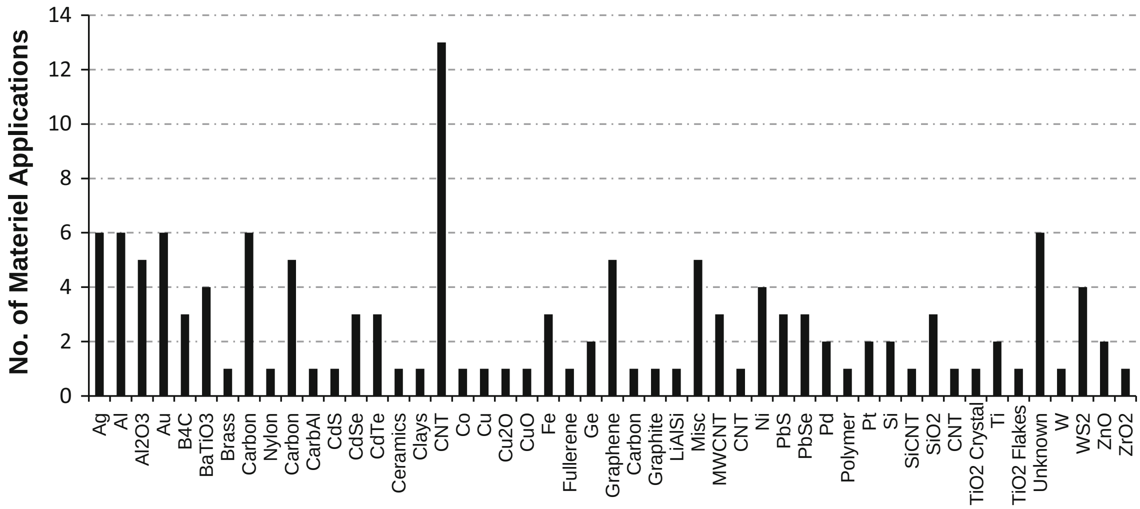

Fig. 1 Distribution of nanomaterials based on the current inventory of 133 unique materiel applications

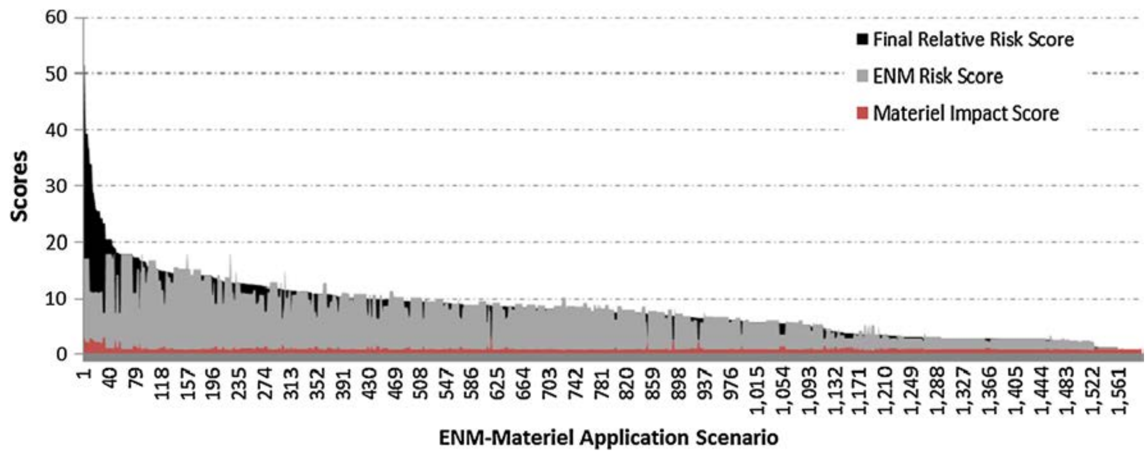

Fig. 2 Baseline relative risks scores of all possible scenarios currently in TEARR (N = 1,596)

Table 3 Summary of relative risk scores for all ENM–Army materiel scenarios in the baseline analysis

Scoring component	Minimum	Maximum[a]	Mean	Variance
ENM risk factor score	1.00	15.68/30	7.80	8.80
Army materiel impact score	0.00	3.29/100	1.06	0.08
Final risk score	0.00	42.84/3,000	8.20	17.73

[a] These scores represent the final ENM risk factor and materiel impact scores (out of the maximum scores possible) which are based on weighted averages across all ENM characteristics or all materiel characteristics, respectively

ingestion exposure routes also ranked high for these Army materiel, based on current knowledge. Additionally, silver (Ag) ranked relatively high in the relative risk scoring for accidental ingestion of Ag-containing Army materiel used in energy and sensor applications, and carbon nanotubes (CNT) also ranked relatively high based on worker inhalation from CNTs used in research and development practices. In contrast, the lowest scoring ENM–materiel pair scenarios (excluding scenarios involving unknown substances) included aluminums, ceramics, and carbon-containing ENMs used in solid matrices (such as armor, vehicles, and personal protection equipment), because the likelihood of these ENMs being released during operational (or even accidental) use was very low, or because

many of the low scoring items had very few end-use items or were still in the development phase.

Across all Army materiel categories based on the average final relative risk score, the 'smokes and obscurants' category had the highest potential risk based on currently available information, with an average score of 19.02 (Fig. 3). Smokes and obscurants incorporate ENMs that were also shown to be more highly ranked, such as aluminum (Al), copper (Cu), brass, and titanium dioxide (TiO_2) (results not shown). The next highest risk Army materiel categories include coolants (average risk score of 11.67) and greases (average risk score of 10.67), containing ENMs such as alumina (Al_2O_3) and CNTs. The categories with the overall lowest risk included rations (3.12), projectiles (2.42), and communication (2.42) with largely unknown ENM composition. The average risk scores for this materiel were relatively low, most likely due to their incorporation into solid matrices or other materiel expected to have low exposure potentials. Several categories also showed zero risk (not shown), predominantly due to a lack of data or information regarding the ENMs being used in those applications.

The five highest ranked ENMs included in TEARR were as follows: copper (Cu) (average risk score of 22.9), brass (15.95), titanium dioxide (TiO2) (14.41), palladium (Pd) (11.46), and silver (Ag) (10.42) (Fig. 4). These ENMs were incorporated into smokes and obscurants, sensors, energy, and imaging (results not shown due to confidentiality reasons; Army-sensitive information). In contrast, the ENMs that were ranked the lowest in TEARR were as follows: silicon (Si) (4.96), carbon aluminum composite (CarbAl) (4.79), ceramics (4.65), miscellaneous (4.32), and unknown ENMs (2.74). These ENMs were used in a wide range of Army materiel: research and development, lubricants, energy, batteries, protection, energetics, coatings and paintings, air filtration and purification, rations, and communication. The average risk scores for these ENMs were most likely due to the low expected exposure potential and a lack of data or information regarding the physicochemical parameters of these ENMs.

3.4 Data sources, uncertainty, and data gaps

The relative risk ranking approach presented here represents a mathematically simple, yet comprehensive, application that facilitates the use of available data and expert judgment, as well as hypothesis testing (e.g., understanding the impact of weighting schemes). Even for relatively simple mathematical constructs such as this ranking tool, reviewing the data sources and underlying uncertainties is critically important to determine what types of research will lead to substantial improvements in the quality of the risk predictions and what input data should be collected and refined. The outcomes from the TEARR framework

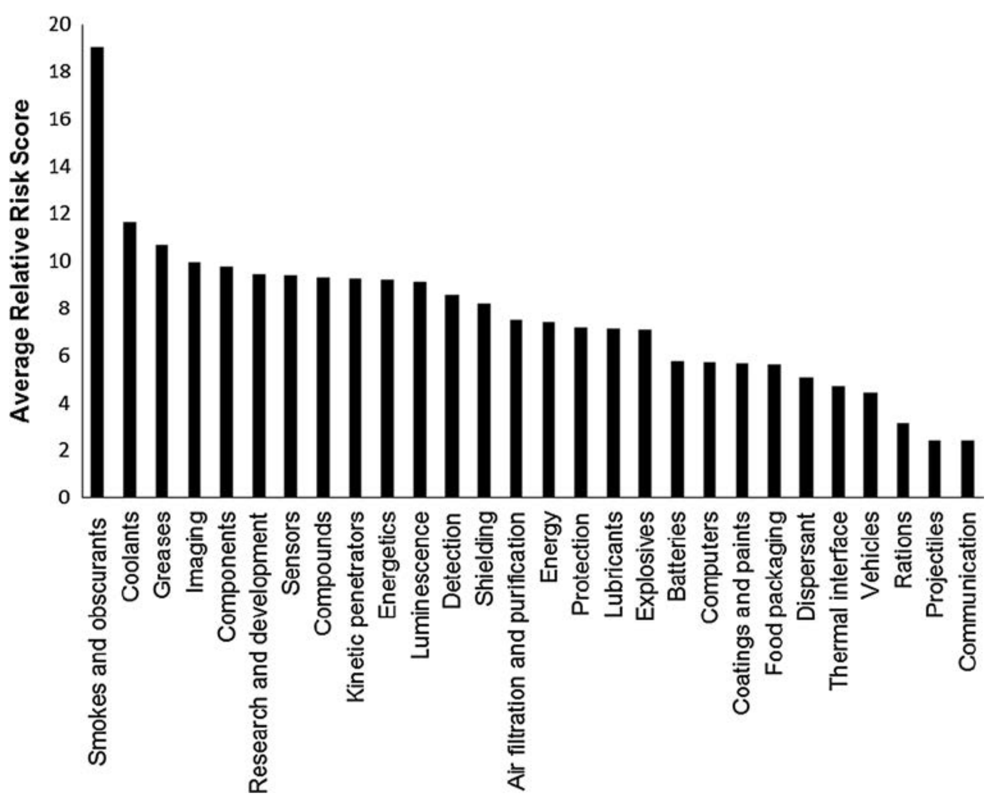

Fig. 3 Average relative risk scores across Army materiel

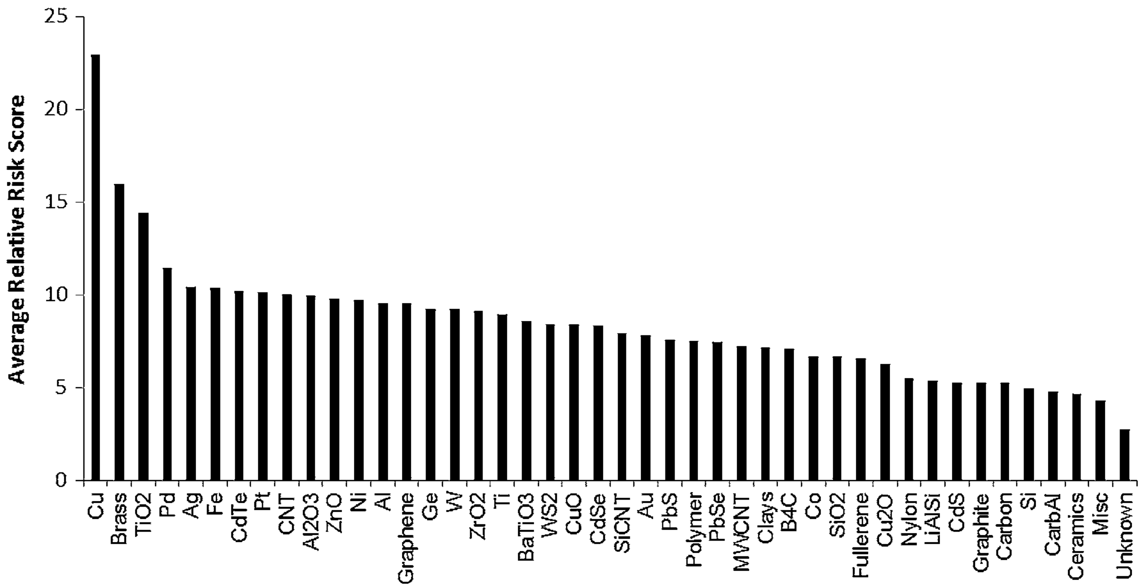

Fig. 4 Average relative risk scores across ENMs

can be used to help identify these data gaps, which in turn could reduce the uncertainties associated with risk rankings, resulting in improved relative risk estimates. It should be noted that the focus here is epistemic uncertainty, or uncertainty that may be reduced from further research as opposed to uncertainties that are stochastic in nature (Grieger et al. 2009).

In TEARR, a review of the data sources used may help compare the relative importance of various uncertainties that may be associated with each source (Figure S5 in SI). The data sources used for each scenario run in TEARR are provided as a percentage of all data sources and act as a final and critical step in the ranking process, especially given the extent of our data gaps and use of four types of data [i.e., Army supplied, literature derived, expert elicitation, or user applied (default)]. In this analysis, expert judgment in the case of Army materiel impact scoring and default scoring in the case of ENM risk scores was predominantly the basis for the scoring in TEARR (Figure S5 in SI). As shown in Figure S5 in SI, 41 % of the Army materiel impact scores were derived from Army-supplied data/information, while 11 % of ENM risk scores were based on literature values, 8 % on expert judgment, and 7 % on Army-supplied data/information. It is envisioned that future applications and modifications to TEARR will include an updated database which will incorporate new data and information from literature sources as it becomes available. For example, the ability to tap into publically accessible databases that focus on the environmental, health, and safety (EHS) implications of ENMs, such as the Nanomaterial Registry (www.nanomaterialregistry.org), would be ideal in order to be able to access (possibly in real time) the most current data set on ENMs in which to update the TEARR database.

In addition to a review of the underlying data sources used in TEARR, the relative risk scores from the baseline analysis appear to be low compared with the maximum possible risk score (i.e., 42.84 out of 3,000). While this could indicate that very few ENM–materiel pairs pose a high risk, a closer look at the data used to support the baseline analysis suggests that our current lack of empirical data led to lower relative risk scores in order to reduce potential biases in the scoring estimates. In other words, the prevalence of data gaps and uncertainties related to ENM and Army materiel characteristics may have erred in the production of false negatives rather than of false positives. Further work and modifications to TEARR, including the incorporation of more data from recently published studies and/or access to publically available databases focused on EHS implications of ENMs, are required in order to refine these baseline results generated thus far.

As stated previously in this analysis, the selection of the seven representative ENM characteristics was performed in order to streamline data collection efforts as well as manage the data gaps related to obtaining data for each of the ENM characteristics for all ENMs in this analysis. In fact, obtaining the remaining 20 non-representative ENM characteristics was extremely challenging, as data gaps were exceedingly prevalent, thus leading to the use of representative ENM characteristics as proxies for the other ENM characteristics in the same category. Even doing this, the seven representative ENM characteristics (size, degradation potential, surface charge/zeta potential, solubility, toxicity, shape, and form) contained data gaps of 10, 25,

48, 21, 23, 32, and 10 %, respectively (as shown in the underlying database, not shown here). While expert elicitation and literature reviews were conducted to reduce data gaps for the initial evaluation, further data collection for these characteristics, particularly toxicity and solubility, as well as data points that relied on bulk-scale materials rather than ENM specifically are still needed. Therefore, the initial relative risk ranking based on the representative ENM characteristics is characterized by substantial uncertainty due to the use of default scores for the remaining ENM characteristics. Considering default ENM characteristics, a significant reduction in the ranking uncertainty (currently defined as source information) could be achieved by obtaining additional ENM-specific data for ENM–materiel pairs, such as surface chemistry, chemical composition, surface reactivity, and partitioning coefficients. It is noted that a substantial amount of ongoing research is currently being conducted to improve test methods to enhance characterization efforts of ENMs, e.g., Oomen et al. (2014), and hence, further refinements and revisions to TEARR will need to incorporate recently published studies.

4 Conclusions and recommendations

This analysis documents the methodology and approach taken to develop and implement a relative risk ranking tool for ENMs in Army materiel applications. The output from this risk ranking tool, TEARR, provides relative risk scores and ranks for ENMs, Army materiel, and ENM–material pairs, thereby identifying the ENMs, materiel, and ENM–materiel pairs which were ranked the highest (and lowest) for further analysis. In order to accomplish this, ENMs and associated Army materiel were identified and inventoried based on collaboration with the Army. Then, a risk ranking algorithm was developed based on ENM and Army materiel characteristics. Finally, the TEARR risk ranking algorithm was implemented and tested on the identified ENMs, materiel, and ENM–materiel pairs, producing relative risk scores and ranks for the ENMs, materiel, and pairs. A total of 45 ENMs, 30 Army materiel, and 133 ENM–materiel pairs were identified in the analysis. Across all ENM–materiel pairs, the maximum relative risk score generated was 42.84 out of a possible 3,000—relatively low—most likely due to the prevalence of data gaps related to the Army materiel impact scores. Therefore, future modifications of TEARR which incorporate new data and information as it arises are clearly needed in order to refine this risk ranking tool.

Across all ENM–materiel pairs included in TEARR, inhalation from accidental exposures to CNTs and copper flakes incorporated into energy and obscurant materiel by Army researchers ranked the highest relative to the other ENM–materiel pairs evaluated in this baseline assessment. Other highly ranked ENM–materiel pairs included accidental ingestion of silver-containing Army materiel used in energy and sensor applications as well as worker inhalation of CNTs used in research and development practices. In addition to these findings, it is also found that data gaps and uncertainties were extremely prevalent across most, if not all, identified ENMs and Army materiel. In order to handle this, several different approaches were taken including the use of representative ENM characteristics to serve as proxies for other ENM characteristics in the same category, the use of expert judgment to elicit ENM risk scores and weights as well as Army materiel impact scores and weights. Furthermore, TEARR was developed in order to allow the incorporation of new or additional data as it becomes available.

The main advantages of TEARR include the ability to provide valuable information related to the potential relative risks associated with ENM–Army materiel pairs based on current knowledge. TEARR also incorporates expert judgment as well as mechanisms to update the underlying baseline database as more knowledge becomes available. Additionally, it is one of the first relative risk ranking tools that incorporate both the unique characteristics of the ENMs in conjunction with the characteristics of the application (i.e., Army materiel in this case) and thereby relevant for more real-world scenarios. The results from TEARR may be used to help prioritize additional research, such as in-depth risk evaluations or further nanotoxicological research pertaining to the highest ranked ENMs, materiel, or ENM–materiel pairs. Finally, the fundamental methodology and risk ranking algorithm developed in TEARR may be applicable to other occupational and environmental settings involving ENMs and therefore easily translated to other application scenarios. Some of the major shortcomings of TEARR primarily involve the uncertainties and data gaps related to the ENMs and Army materiel. As any risk ranking or analysis tool is subject to the quality of the data stored within, so is the TEARR database and risk ranking tool, in that the results are highly dependent upon the quality of the underlying data. It appears that the relative risk scores may be heavily influenced by the uncertainties and data gaps related to the Army materiel impact scores, producing lower than expected risk ranking results. Thus, further modifications to TEARR which rely on updated information are clearly needed. Furthermore, expert elicitation based on a total of two nanotoxicology and ENM risk experts was used as a basis to score the ENM risk scores and weights as well as Army materiel impact scores and weights. In comparison, a larger expert elicitation panel (i.e., 6–10 experts) in fields of nanotoxicology and ENM risk analysis would be ideal.

In light of these findings, it is recommended that future revisions of TEARR and other relative risk ranking tools

involving ENMs be able to tap into publically accessible databases, such as the Nanomaterial Registry, in order to be able to update the underlying data sets on EHS implications of ENMs, potentially in real time. As significant research efforts are currently focused on the collection and curation of data on ENMs and their behavior, risk ranking tools such as TEARR would benefit from accessing these publically accessible databases. Separate analyses that assess "new" levels of uncertainty if additional data were required, such as Value of Information methodologies (e.g., Linkov et al. 2011), may also be beneficial when considering such updates based on current knowledge. In addition to these recommendations, it is also recommended that increased funding is made available to support the development of decision support tools for emerging technologies, including those focused on risk ranking, which specialize in conditions of extreme uncertainty. Given the ever-increasing pace of ENM development and incorporation into various products applications as well as the extreme challenges to develop the data required to satisfy quantitative risk assessment approaches, decision support frameworks which focus on handling extreme conditions of uncertainty in a transparent, structured, and robust manner are critically needed, particularly for decisions regarding emerging technologies in the twenty-first century.

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